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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 11/19/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/910,702

Applicant(s)

KONRADI ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 4, 5, 15, and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-14, and 17-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-3, 6-14, and 17-27) in Paper No. 13 is acknowledged. The traversal is on the ground(s) that:

- a. Restriction requirement as to Groups 1-27 is inconsistent with Patent Office's stated guidelines regarding restriction of Markush Groups
- b. Examination of all of the claims would not impose a serious burden on the examiner.

This is not found persuasive for the following reasons:

- Each group of the restriction still allows for a Markush group though with a more limited scope. While it may be true that many of the subgenera would not be described in the specification, the examiner is still obligated to search each subgenus. Furthermore, the description of a subgenus does not constitute a basis for whether a restriction should be made.
- Formulae (Ia) and (Ib) allow for a plethora of compounds having only $-N-CH_2-C(=O)$ as a common core. Such a core alone does not define the invention. It is the combination of many variables such as Ar^1 , CH_2-Ar^2 , ring B or C, that defines each group of compounds. Therefore, a reference that anticipated on one group would not do so to the other groups.
- Therefore, the search for group I would not be required for other groups, and thus, **a burden of searching** exists.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 1-3, 6-14, and 17-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation and use of compounds having pyridone, pyrimidone, thiadiazole, pyridazine, pyrimidine, or pyrazine, does **not** reasonably provide **enablement** for compounds having **other heteroaryl** groups [defined for Ar¹, Ar², B, or C]. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

a. **The breadth of the claims:** The scope of “heteroaryl”, or “heterocyclic” group, recited for variables Ar¹, Ar², B, or C, encompasses many ring and ring systems that have no enablement in the instant specification.

b. **The amount of direction or guidance presented:** The specification does not appear to provide enablement for making compounds having a heteroaryl groups other than pyrimidine, pyridone. Schemes II-V generically teach how to make compounds of formulae (Ia) or (Ib) with starting materials of A'-NH₂, or A''-X³ (wherein A' or A'' is a heteroaryl group). However, the specification does not appear to disclose how such as starting material can be prepared or obtained. Regarding working examples, there is only one example in which (apparently) a compound of formula IIc is made, and tested for the activity on VLA-4. Thus, following the available guidance, one skilled in the art can only make and use compound of formula IIc.

c. **The state of the prior art:** No reference is found that could guide the skilled chemist in the preparation of a compound of the instant formula Ia, Ib, IIa, or IIc.

Because of the structural difference, the biological activity of the tested compound cannot be extrapolated to those having other heteroaryl groups as a substituent defined by Ar¹, Ar², B or C.

Thus, with the unpredictable nature of the art, and the limited guidance, one skilled in the art would have to carry out undue experimentation to make and use compounds having a

heteroaryl group other than pyrimidin, pyridone, pyrimidinone, thiadiazole, pyridazine or pyrazine [as defined for Ar¹, Ar², B or C].

3. **Scope of Enablement:** Claims 20, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating asthma and allograft rejection, does not reasonably provide enablement for other diseases that are allegedly mediated by VLA-4 (including those have not been discovered). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The scope of a "method for treating a disease mediated by VLA-4" encompasses treatment for diseases of inflammation and those that have not been discovered. The specification only provides testing for asthma and allograft rejection. Although inflammation can affect many organs and tissues, the established treatment for one or two conditions does not sufficiently allow one skilled in the art to apply the same compounds in the treatment of other inflammatory conditions. For example, currently the asthma drug such as: Proventil, or theophylline is used to treat asthma, but it is not used to treat arthritis or other skin diseases that are caused by inflammatory reaction. Therefore, if a compound can treat one condition of inflammation, does not mean it can treat all conditions of inflammation since each condition is involved different pathophysiology.

Again with the unpredictable nature of the art, the skilled clinician will have to carry out undue experimentation to treat other conditions mediated by VLA-4.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (7 am -12 pm, and 3 pm - 6 pm) starting from 10-1st -03.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong

November 16, 2003



ALAN L. ROTMAN
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